PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Public subsidies and the recommendation of child vaccines among primary care physicians: a nationwide cross-sectional study in Japan
AUTHORS	Sakanishi, Yuta; Yamamoto, Yosuke; Hara, Megumi; Fukumori, Norio; Goto, Yoshihito; Kusaba, Tesshu; Tanaka, Keitaro; Sugioka, Takashi; Japan Primary Care Association, Vaccine Project Team; Fukuhara, Shunichi

VERSION 1 – REVIEW

REVIEWER	James H. Conway, MD Professor of Pediatrics, Pediatric Infectious Diseases Training Program Director, Associate Director for Health Sciences - Global Health Institute, University of Wisconsin-Madison, School of Medicine & Public Health, USA
REVIEW RETURNED	27-Jan-2018

GENERAL COMMENTS	The authors have presented a preliminary analysis examining whether knowledge of subsidies affect strength of vaccine recommendations in Japanese primary care providers. They include appropriate statistical analysis describing demographic features associated with stronger recommendations. While the data is nearly 5 years old, it is still pertinent in describing the role that knowledge gaps may have. This paper does offer some important information that does improve overall immunization knowledge, which could be broadly applicable - as my experience is that many primary care physicians in many countries are unaware of how vaccine finance works in their own region. For a reviewer who is not familiar with the history of Japanese vaccine programs, there are a few critical pieces of information that would improve this manuscript: 1) While it is good to know when each of the study vaccines were first offered, it would also be important to know the timing for when subsidies were provided for each. Did this happen at vaccine offering, or later? Were these subsidies implemented for all 3 vaccines at the same time or different dates. 2) How substantial are these subsidies? Are they available to all patients or only certain socioeconomic groups? 3) Were the respondents from one geographic area or distributed across the country? 4) What is/was the estimated coverage rates for each of these 3 vaccines in 2012? 5) When subsidies are offered/added to the immunization programs, how is that information currently conveyed to patients/families and providers?

REVIEWER	Abram Wagner University of Michigan, USA

REVIEW RETURNED	05-Mar-2018

GENERAL COMMENTS	This is an excellent study about why physicians in Japan recommend Hib, PCV, or HPV vaccines – which are all subsidized but which are not mandatory and have low uptake. I only have minor concerns below: Abstract : I would change the results' first sentence to include info on the original sample size of 2,880, and therefore the response rate of 25.8% Introduction: page 6 line 33: I would say "mandatory" and not "routine". To me, routine immunization services just refers to any immunization given in a public health department or by a PCP. (see also line 36) It might help to mention what a "mandatory" vaccine means in japan (is it mandatory prior to school/daycare entry? are there any waivers? does this vary across local governments) could you include information on when PCV, Hib, and HPV entered the market in Japan? (for instance when were they first on private market, and then when were they started being subsidized?) do you have any more recent information on Hib, PCV, or HPV coverage? (you mention in page 6 line 45 about Hib coverage in 2010) By subsidy do you mean these vaccines are completely free? Or is there a co-pay or administration cost? Methods: Was the survey administered online or by mail or in person? Results: I don't think PGY is a common abbreviation and I'd prefer if you just wrote it out. Table 2 is a bit confusing, but has good information. I would put the "total" column (now the last one), as the second column (and not under "recommendation level for each vaccine), and then for always recommend to not recommend, for these columns, I would have them each add up to 100% (e.g., always recommend for Hib vaccine awareness (+) would be "221 (67.5%)" because 221/327 = 67.5%. Also note, my preference within all tables is to include % signs after each percentage – even if within parenthesis and if table heading shows this. it just makes the numbers more readable – however, this is up to you to make this change or not.

VERSION 1 – AUTHOR RESPONSE

RESPONSE TO REVIEWER 1:

We wish to express our appreciation to Reviewer 1 for the insightful comments. These have helped us to significantly improve our manuscript.

Comment1: While it is good to know when each of the study vaccines were first offered, it would also be important to know the timing for when subsidies were provided for each. Did this happen at vaccine offering, or later? Were these subsidies implemented for all 3 vaccines at the same time or different dates.

Response: Thank you for your comment. These vaccines were introduced in Japan in the following years: Hib in 2008, PCV in 2010, and bivalent HPV in 2009. There were no public subsidies for them at the time they were initially offered. The Government of Japan implemented subsidies for local governments for the fees for these three vaccines from November 2010. Thus, the subsidies were provided after the vaccines were first offered, and were implemented for all three vaccines at the same time.14

Accordingly, we have added the following text on p. 6, lines 11–12.

These vaccines were introduced in Japan in the following years: Hib in 2008, PCV in 2010, and bivalent HPV in 2009. There were no public subsidies for them at the time they were initially offered.

We also changed the following text on p. 7, line 5.

Therefore, the Government of Japan implemented subsidies for local governments for Hib, PCV, and HPV vaccine fees from November 2010.

to

Therefore, the Government of Japan implemented subsidies for local governments for Hib, PCV, and HPV vaccine fees from November 2010, all at the same time.14

Comment 2: How substantial are these subsidies? Are they available to all patients or only certain socioeconomic groups?

Response: The subsidies were available to all patients. They were intended for all children aged over 2 months and under 5 years for Hib and PCV, and all girls aged 12–16 years for the HPV vaccine.15

Accordingly, we added the following text on p. 7, lines 5-7.

The subsidies were intended for all children aged over 2 months and under 5 years for Hib and PCV, and all girls aged 12–16 years for HPV.15 Local governments determined the subsidy amounts.

Comment 3: Were the respondents from one geographic area or distributed across the country?

Response: The respondents were from all 47 prefectures of Japan. Accordingly, we added the following text on p. 11, lines 9-10.

The respondents were from all 47 prefectures of Japan.

Comment 4: What is/was the estimated coverage rates for each of these 3 vaccines in 2012?

Response: The estimated coverage rates for these vaccines in 2012 were 70%–90% for Hib,29 30 80%–90% for PCV,29 31 and 65%–75% for HPV.32 33

Accordingly, we added the following text on p. 20, lines 2–4.

The estimated coverage rates for these vaccines in 2012 were 70%–90% for Hib,29 30 80%–90% for PCV,29 31 and 65%–75% for HPV.32 33

Comment 5: When subsidies are offered/added to the immunization programs, how is that information currently conveyed to patients/families and providers?

Response: At these times, the information was conveyed to patients/families and providers though public outlets such as local government websites or public relations magazines. Additionally, public health nurses informed parents at the time the children received health check-ups. Local governments also sent notices about the subsidies to each medical facility and medical association.

Accordingly, we added the following text on p. 19, lines 14–18.

When subsidies were offered, information about them was conveyed to patients/families and providers though public outlets such as local government websites or public relations magazines. Additionally, public health nurses informed parents at the time the children received health check-ups. Local governments also sent notices about the subsidies to each medical facility and medical association.

We wish to thank the Reviewer again for the valuable comments.

RESPONSE TO REVIEWER 2:

We wish to express our appreciation to Reviewer 2 for the insightful comments. These helped us to considerably improve our manuscript.

Comment 1: Abstract : I would change the results' first sentence to include info on the original sample size of 2,880, and therefore the response rate of 25.8%

Response: We appreciate this comment. Accordingly, we added the following text on p. 4, line 3.

The response rate was 25.8% (743/2,880).

Comment2: Introduction: page 6 line 33: I would say "mandatory" and not "routine". To me, routine immunization services just refers to any immunization given in a public health department or by a PCP. (see also line 36)
It might help to mention what a "mandatory" vaccine means in japan (is it mandatory prior to school/daycare entry? are there any waivers? does this vary across local governments)

Response: Thank you very much for the comment. To clarify, routine vaccinations in Japan are not mandatory, but the Japanese government strongly recommends Japanese citizens receive them. We have sought to additionally address this aspect.

We added the following text on p. 6, lines 14–18.

Routine vaccinations are defined by the Preventive Vaccination Law and scheduled in the National Immunization Program. These vaccinations are not mandatory, though the Government of Japan

strongly recommends them. In principle, vaccinations are administered individually, mainly funded by the national and local governments, and are free of charge to recipients at private or public facilities at the request of the local government.9 10

Comment 3: Could you include information on when PCV, Hib, and HPV entered the market in Japan? (for instance when were they first on private market, and then when were they started being subsidized?)
Do you have any more recent information on Hib, PCV, or HPV coverage? (you mention in page 6 line 45 about Hib coverage in 2010)

Response: Thank you for your comment. We added the years these vaccines were introduced in Japan and the coverage of these vaccines in 2012, as follows.

We added the following text on p. 6, lines 11–12.

These vaccines were introduced in Japan in the following years: Hib in 2008, PCV in 2010, and bivalent HPV in 2009. There were no public subsidies for them at the time they were initially offered.

We also added the following text on p. 20, lines 2–4.

The estimated coverage rates for these vaccines in 2012 were 70%–90% for Hib,29 30 80%–90% for PCV,29 31 and 65%–75% for HPV.32 33

Comment 4: By subsidy do you mean these vaccines are completely free? Or is there a co-pay or administration cost?

Response: The subsidies were from the national and local governments; the latter determined the amounts. Most of subsidies were estimated as “full subsidy,” meaning they were free, though we had no confirming information for that. We therefore investigated the type of subsidy (full or not); this was mentioned in the Methods on p. 10, lines 5-7.

Accordingly, we added the following text on p. 7, lines 5–7.

The subsidies were intended for all children aged over 2 months and under 5 years for Hib and PCV, and all girls aged 12 to 16 years for HPV vaccine. Local governments determined the subsidy amounts.

Comment 5: Methods: Was the survey administered online or by mail or in person?

Response: We sent the questionnaires by postal mail. Accordingly we added the following text on p. 8, line 14.

Questionnaires were sent to each participant by postal mail.

Comment 6: Results: I don’t think PGY is a common abbreviation and I’d prefer if you just wrote it out.

Response: Thank you for your advice. Accordingly, we changed “PGY” to “postgraduate year”, on p. 8, line 9; p. 9, line 16; p. 10, line 14; p. 11, line 12; p. 13, line 6; p. 15, line 9; p. 17, line 8; p. 21, lines 15 and 17; and p. 22, line 13.

Comment 7: Table 2 is a bit confusing, but has good information. I would put the “total” column (now the last one), as the second column (and not under “recommendation level for each vaccine), and then for always recommend to not recommend, for these columns, I would have them each add up to 100% (e.g., always recommend for Hib vaccine awareness (+) would be “221 (67.5%)” because 221/327 = 67.5%.

Response: Thank you for the comment. We now realize Table 2 was somewhat confusing. In accordance with the comment, we have revised the table. Additionally, in Table 2, the total number for awareness of the subsidy for PCV vaccine and the proportion of the total “Always Recommend” for the PCV vaccine were incorrect. We revised these accordingly.

We changed Table 2, p. 13, lines 7–8.

We also changed the following text from p. 15, line 4.

Overall, 314 (72.4%) PCPs reported awareness of a public subsidy and 235 (54.2%) recommended the vaccine.

to

Overall, 315 (72.6%) PCPs reported awareness of a public subsidy and 235 (54.1%) recommended the vaccine.

Comment 8: Also note, my preference within all tables is to include % signs after each percentage – even if within parenthesis and if table heading shows this. it just makes the numbers more readable – however, this is up to you to make this change or not.

Response: Thank you for your advice. We agree with your suggestion. Accordingly, we added % signs after each percentage.

Accordingly, we added % signs after each percentage in Table 1 (p. 12), Table 2 (p. 13), Table 3 (p. 14), Table 4 (p. 16), and Table 5 (p. 18).

We wish to thank the Reviewer again for the valuable comments.

References

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・ 10. Saitoh A, Okabe N. Recent progress and concerns regarding the Japanese immunization program: addressing the "vaccine gap". Vaccine 2014;32(34):4253-8. doi: 10.1016/j.vaccine.2014.06.022 [published Online First: 2014/06/22]

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・ 31. Chiba N, Morozumi M, Shouji M, et al. Changes in capsule and drug resistance of Pneumococci after introduction of PCV7, Japan, 2010-2013. Emerg Infect Dis 2014;20(7):1132-9. doi: 10.3201/eid2007.131485 [published Online First: 2014/06/25 06:00]
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・ 33. Yagi A, Ueda Y, Egawa-Takata T, et al. Realistic fear of cervical cancer risk in Japan depending on birth year. Human vaccines & immunotherapeutics 2017;13(7):1700-04. doi: 10.1080/21645515.2017.1292190 [published Online First: 2017/03/09 06:00]

VERSION 2 – REVIEW

REVIEWER	Abram Wagner University of Michigan, USA
REVIEW RETURNED	11-Apr-2018

GENERAL COMMENTS	The authors responded appropriately to reviewer comments, and the manuscript is in good shape.

REVIEWER	James H. Conway University of Wisconsin - School of Medicine & Public Health, USA
REVIEW RETURNED	28-Apr-2018

GENERAL COMMENTS	The revised manuscript is now much clearer, and more widely applicable as well. Clarifying the Japanese immunization subsidy system and the history related to the vaccines studied here, as well as more information about the study participants, makes the information more significant to readers outside Japan - but also helps provide more obvious 'action items' for individuals working to improve immunization coverage rates in Japan.

VERSION 2 – AUTHOR RESPONSE

RESPONSE TO REVIEWER 1:

We wish to express our appreciation to Reviewer 1 for the insightful comments. These have helped us to further improve our manuscript.

Comment1: The revised manuscript is now much clearer, and more widely applicable as well. Clarifying the Japanese immunization subsidy system and the history related to the vaccines studied here, as well as more information about the study participants, makes the information more significant to readers outside Japan - but also helps provide more obvious 'action items' for individuals working to improve immunization coverage rates in Japan.

Response: Thank you for your comments. As we described in the Introduction section, routine vaccinations are mainly funded by the national and local governments, and are free of charge for recipients at private or public facilities, at the request of the local government. Voluntary vaccinations, however, are not subsidized by the national government. Coverage of voluntary vaccinations is much lower and some diseases they target are endemic in the population.

To further clarify this, we have added the following text on p. 6, lines 11-12 and p. 7, lines 4.

In Japan, however, many important vaccines, including Hib, Streptococcus pneumoniae (7-valent pneumococcal conjugate vaccine: PCV), and human papillomavirus (HPV) were voluntary rather than routine, and voluntary vaccinations were not covered by the National Immunization Program, without subsidies by the Government of Japan.

However, coverage of voluntary vaccinations is much lower and some diseases those vaccinations target are endemic in the population.

Regarding the history of the subsidies related to the vaccines studied, we gave details in the Introduction section that these vaccines were introduced in Japan in the following years: Hib in 2008, PCV in 2010, and bivalent HPV in 2009. There were no public subsidies for them at the time they were initially offered. The Government of Japan implemented subsidies for local governments for the fees for these three vaccines from November 2010. Thus, the subsidies were provided after the vaccines were first offered, and were implemented for all three vaccines at the same time.

Study participants were physician members of the Japan Primary Care Association (JPCA). The majority were internists working as primary care physicians at a clinic or hospital.

Accordingly, we have added the following text on p. 8, lines 4-5.

This study used a cross-sectional design with data drawn from a questionnaire conducted by the Japan Primary Care Association (JPCA), the largest academic association for PCPs in Japan. The majority of the JPCA physician members were internists working as PCPs at a clinic or hospital.

Thank you again for your valuable comments.

RESPONSE TO REVIEWER 2:

We wish to express our appreciation to Reviewer 2 for this comment.

Comment 1: The authors responded appropriately to reviewer comments, and the manuscript is in good shape.

Response: Thank you very much. We appreciate your positive word